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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,975	07/30/2003	James Hunter Boone	TLAB.79219	9513

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/629,975	BOONE ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Amendment Entry

1. Applicants response to the Office Action mailed December 16, 2004 is acknowledged (paper filed March 21, 2005). In the amendment filed therein the specification along with claims 1, 2 and 3 were modified. Currently, claims 1-6 are pending and currently under consideration.

2. Rejections and/or objections of record not reiterated below have been withdrawn.

OBJECTIONS WITHDRAWN

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

Response to Arguments

Applicant contends that all references cited in the specification were properly submitted by way of an Information Disclosure Statement in parent application US Serial No.10/002,842. The IDS in parent application US Serial No.10/002,842 has been considered. It is not necessary for Applicant to submit a separate IDS in the present application. See MPEP 609. The objection is withdrawn.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and indefinite in reciting "total" endogenous lactoferrin because it is not clear as to what the term "total" encompasses. As recited the metes and bounds of the claim cannot be determined. The term "total" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Is it applicant's intent to mean that all the lactoferrin (whole and half-sized) found in the sample will be detected? Please clarify.

B. The term "within a linear portion" in claim 2 is a relative term which renders the claim indefinite. It is not clear as to what applicant considers a linear portion of the standard curve. Will any measurement on the standard curve meet the instantly claimed limitation? The term "within a linear portion" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In order to obviate this rejection it is suggested that "within a linear portion" be removed from the claim.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Sugi et al. (The American Journal of Gastroenterology, Vol.91, No.5, 927-934, 1996).

Sugi et al. disclose that lactoferrin (LF) levels were elevated in fecal samples of patients with inflammatory bowel disease. See abstract. The ELISA assay procedure is disclosed on page 928. LF elevation was seen in various disease states. Sugi et al. measure multiple samples at different times (1st and 2nd samples wherein the second sample concentration is measured at a time later than the first sample measurement). In particular the multiple sampling analysis is seen on page 929 in figure 2 for example. LF concentrations are measured at different time intervals, which include 24hours, 48hours, 72hours, and 96hours. The LF concentrations are subsequently compared to each other in figure 2 – A, B, and C (48hrs – 72hours –96 hours are all later than the first 24hour LF detection).

Response to Arguments

Applicant contends that Sugi et al. do not describe each and every element set forth in the rejected claims.

Specifically applicant argues that Sugi et al. teach a method of reading the same fecal sample at a first time and a second time, while the instant method detects different samples at a first and second time. This argument was carefully considered but not found persuasive because Sugi et al. disclose the collection of different samples (from various patients) at times varying from 48 to 72 hours (the samples are not all the same). See page 928 1st column last paragraph – Subjects to 2nd column 2nd paragraph – Method of stool collection.

Also, the claims do not require different 1st and 2nd samples. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., different 1st and 2nd samples) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 1-3 are rejected under 35 U.S.C.103(a) as being unpatentable over Uchida et al. (US Patent #5,552,292).

Uchida et al. teach methods to measure lactoferrin in fecal samples. Lactoferrin is taught to be a marker for various diseases related to inflammatory gastrointestinal disorders and colon cancer. Column 2 lines 46-59. Lactoferrin was found to be the most stable substance in feces. Column 3 lines 10-11. Specifically a polyclonal antibody for lactoferrin (DAKOPATT) is employed to measure lactoferrin in inflammatory diarrhea specimens. Column 5 lines 57-61.

The method was performed in an enzyme-linked immunoassay format. A polyclonal antibody against lactoferrin (anti-human lactoferrin antibody) is immobilized onto wells of a 96-well polystyrene micro plate. The plate is contacted with diluted fecal specimen (column 11 lines 31-33 wherein 50Tl of sample is added to 100Tl %1BSA and TBS buffer) and detected with a polyclonal antibody labeled with alkaline phosphatase (anti-human-lactoferrin antibody). See column 11 example 2 and column 5 lines 14-19. The results were correlated to standards prepared with purified lactoferrin. Column 6 lines 13-19.

The assay results were detected at 510/630nm absorbance. Column 11 lines 53-56. Increased levels of lactoferrin were demonstrated to several diseases. See column 12-Results.

Uchida et al. disclose standard curve comparative analyses (claim 2). Healthy person fecal samples were run and graphed on a curve for comparison to unknown sample sets (standard curve). Column 7 lines 51-64 and column 8 lines 18-29.

Kit embodiments are also disclosed. The kit contains antibodies immobilized on a solid phase (micro plate), an enzyme linked antibody, and a chromogene (enzyme substrate for color development). See column 4 lines 1-9 and column 5 lines 36-40.

With respect to endogenous lactoferrin, it is noted that the lactoferrin detected by Uchida et al. were found within the patient (endogenous to the patient) and occurred as a result of disorders. Normal patients exhibited very small amounts of lactoferrin (0.75 – 2.4Tg/g feces) and Uchida et al. taught that their method could be used in various types of lactoferrin (column 6 lines 58-61). Therefore absent evidence to the contrary Uchida et al. teach the detection of endogenous lactoferrin.

Uchida et al. differ fro the instant invention in not specifically teaching sample detection at 450nm. However, Uchida et al. teach that the absorbance measurement is routinely adjusted to optimize the assay. See column 5 lines 30-32. Absent evidence to the contrary the detection of the lactoferrin assay taught by Uchida et al. is routine optimization. It would have been obvious to one having ordinary skill in the art at the time of the invention was made to measure lactoferrin at a 450nm absorbance reading, since it has been held that discovering an optimal value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205, USPQ 215(CCPA 1980).

III. Claims 4 and 5 are rejected under 35 U.S.C.103(a) as being unpatentable over Uchida et al. (US Patent #5,552,292) in view of Foster et al. (U.S. Patent#4,444,879).

Please see Uchida et al. as set forth above.

Although Uchida et al. teach the regents required by the claims, they do not specifically teach the inclusion of all the reagents in kit configurations (in particularly the purified human lactoferrin – taught in '292 column in column 6 lines 14-16 and stop solution or coloring reagent – taught in '292 column 5 line 29-30). In other words, the reference fails to teach all the reagents as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a micro plate, positive controls, negative controls, standards, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents as taught by Uchida et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

Response to Arguments

Applicant contends that the Uchida reference fails to teach or suggest all the limitations of the rejected claims.

Specifically applicant argues that Uchida measures the level of only whole-sized lactoferrin by immunoassay utilizing monoclonal antibodies. This argument was carefully considered but not found persuasive because Uchida discloses the detection of total lactoferrin (whole and half-sized) with a polyclonal antibody. Lactoferrin was measured by immunoassay utilizing polyclonal antibody (DAKOPATT, Denmark, referred to as DAKO). The results showed two types of lactoferrin; whole and half-sized. See column 5 lines 57 through column 6 line 2.

Applicant further argues that the Uchida reference indicates that various types of lactoferrin were tested but "only the whole-sized lactoferrin. . . . in feces should be measured for screening of gastrointestinal tract disorders. Applicants cite col 7, lines 3-8. This argument was carefully considered but not found persuasive because Uchida teaches that lactoferrin [total] is a marker for inflammatory gastrointestinal disorders and the distinction between invasive/inflammatory diarrhea. See column 1 lines 54-66.

In response to the argument that Uchida fails to teach or suggest the determination of an optical density at 450nm as recited in amended claim 1, it is noted that a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. In re Boe, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). In re Chapman, 357 F.2d 418, 148 USPQ 711 (CCPA 1966). Uchida teaches "that the absorbance measurement is routinely adjusted to optimize the assay". Column 5 lines 30-32.

Absent evidence to the contrary, the provision of adjustability, where needed, involves only routine skill in the art. In re Stevens, 101 USPQ 284(CCPA 1954).

Applicant argues that Uchida employs a wavelength at 510/630nm while the instant invention uses a wavelength of 450nm, this argument was carefully considered but not found persuasive because the test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See, *In re Bent*, 52 CCPA 850, 144 USPQ 28 (1964); *In re Nievelt*, 179 USPQ 224 (CCPA 1973). Uchida teaches "that the absorbance measurement is routinely adjusted to optimize the assay". Column 5 lines 30-32.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant contends that the rejections under 103(a) including Foster 4,444,879 should be withdrawn because of the deficiencies noted in Uchida et al. The deficiencies in Uchida et al. have been addressed above. Accordingly, the rejections are maintained.

7. For reasons aforementioned, no claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

9. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Tabata et al. (Rinsho Byori, 1997, 45(12), 1201-1203 – Abstract Only) teach that lactoferrin is useful in monitoring inflammatory bowel disease.

B. Mathias et al. (Digestive Diseases and Sciences, June 1994, Vol.39, No.6, 1155-1162) disclose methods for assessing bowel disease detecting duplicate patient samples to allow for test drug assessment (leuprolide). See abstract and page 1160-Discussion.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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